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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,691	07/20/2001	Ping Gao	28341/00222.US1	9971

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EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/05/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/909,691	Applicant(s) GAO ET AL.	
	Examiner Lakshmi S Channavajjala	Art Unit 1615	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-35* is/are pending in the application.

4a) Of the above claim(s) *21-24 and 28-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-20 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Request for extension of time and amendment A dated 6-18-03 is acknowledged. Claim 5 has been canceled. Claims 1-4 and 6-35 are pending. Claims 21-24 and 28-35 have been withdrawn from consideration as being non-elected. Claims 1-4, 6-20 and 25-27 are being examined.

The following rejection has been maintained:

Claim Rejections - 35 USC § 103

Claims 1-4, 6-20 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of the following combination of references:

1. WO 96/03113 (WO '113) in view of US 5,866,159 to Hauer et al (hereafter Hauer)

2. Hauer in view of WO '113 or

4. Hauer in view of WO 99WO '848.

Instant claims are directed to a self-emulsifying drug delivery (SEDD) system comprising an extremely water-insoluble lipophilic active agent, a fatty aid, a surfactant and polyvinylpyrrolidone (PVP), wherein the weight ratio of fatty acid to PVP is 2:1 to 1:3. Dependent claims further limit the ratio of surfactant to PVP; recite specific surfactants, fatty acids, active agents etc.

WO '113 teaches a SEDD system for increasing bioavailability of water insoluble or oil soluble drugs, comprising the 0.1% t 17% drug, 2% to 50% of a solubilizer, 10% to 55% of an emulsifier and oil (claim 1 and pages 6-7, page 8, lines 14-24). Particularly, WO '113 teaches the claimed emulsifiers (page 7) and their solubilizers include fatty acids such as oleic acid, linoeic acid (lines bridging pages 7-8). WO' 113 also teaches oral administration of their composition in

the form of gelatin capsules (page 8, lines 25-28). WO does not teach PVP of the instant claims and also fails to teach specific drugs of claim 20.

Hauer teaches microemulsion preconcentrate compositions containing highly water insoluble drug such as cyclosporin, which is suitable for oral as well as topical admninistration (abstract, col. 3, lines 23-25). In addition to cyclosporin, the composition of Hauer further comprises surfactant (col. 9, lines 34 through col. 12, lines 34), a hydrophilic phase containing propylene glycol or tetrahydrofuryl ether of polyoxyalkanediol (col. 7), lipophilic phase comprising fatty acid triglycerides (col. 9) and a thickening agent (col. 12, lines 35-col. 13, lines 19). In particular, example 29 of Hauer recites claimed surfactants and PVP, with the ratios of surfactants to PVP being within t he claimed limits.

WO '848 teaches self-emulsifying dosage forms of water-insoluble anticancer drugs such as paclitaxel, wherein the composition comprises a hydrophobic component comprising triglycerides, free fatty acids etc., surfactants, and hydrophilic components such as polyethylene glycol. The surfactants, fatty acids etc., described by WO '848 (pages 4-5 and example 5) read on the instant claimed components. WO '848 fails to teach PVP in their compositions.

Thus, all the three references described above are directed to achieving increased bioavailability of highly water insoluble drugs and teach pre-concentrate of emulsion, which is the same as SEDD systems. It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to add PVP of Hauer, as a thickening agent, in the SEDD system of WO '113 or WO '848 because Hauer teaches that thickening agents such as PVP are capable of modifying the release characteristics of the lipophilic drug (col. 20, lines 53 though col. 21, lines 1-4). Alternatively, it would have been obvious for one of an ordinary skill in the art at the

time of the instant invention to add fatty acids of WO '113 or WO '848 to the pre-emulsion concentrate of Hauer because WO '113 teaches fatty acids for solubilizing a substantially insoluble lipophilic drug, without any toxic side effects and WO '848 teach equivalence of fatty acids such as linoeic acid and triglycerides in the SEDD system for administering and improving bioavailability of lipophilic drugs. The above references do not teach the exact ratios of PVP and fatty acids. However, optimizing the ratios of individual components with their art recognized effect would have been within the gambit one of an ordinary skill in the art. Accordingly, a skilled artisan would have optimized the ratios of PVP and fatty acids as well as PVP and surfactants with an expectation to achieve the maximum desired bioavailability and a desired release pattern of a highly water-insoluble lipophilic drug.

Response to Arguments

Applicant's arguments filed 6-18-03 have been fully considered but they are not persuasive.

Applicants argue Hauer teaches high molecular weight PVP as a thickening agent and fails to teach the low molecular weight PVP and in particular, for dissolution of highly lipophilic active agent. Applicants argue that the recited formulation (with low MW PVP) provides high bioavailability in the administration of extremely water-insoluble active agents. However, examiner notes that instant claims composition claims are not limited to increasing the solubility of lipophilic active agents. In addition, claim 4 still recites high molecular weight PVP i.e., up to 100,000. Instant specification (page 7, lines 21-33) also states that a PVP useful in the present invention i.e., for dissolution of lipophilic agents, can have a MW in the range of 2,500 to

100,000 (including Kolloidon (PVP) 30 and 90, described and exemplified by Hauer), suggesting that the solubility of lipophilic agents can be enhanced using a PVP of any MW in the above range. With respect to applicants' arguments that the high MW PVP only thickens and does not enhance solubility, applicants have shown any negative effect of high MW PVP on the dissolution of lipophilic agents. The instant claimed PVP with a MW of 2,500 to 20,000 correspond to K value of 12-25 (a measure of viscosity), thus showing that increasing viscosity would still render the lipophilic agents soluble (instant page 8, lines 32-33). Therefore, the rejection has been maintained.

The following is a new rejection in view of the amendment:

Claim Rejections - 35 USC § 112

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Instant claim recites the molecular weight of PVP in the range of 2,500 to 100,000. However claim 1, from which the instant claim is dependent upon only recites the molecular weight in the range of 2,500 to 20,000. It is unclear as to what range of molecular weights applicants intend to claim. A clarification and appropriate corrected is requested.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

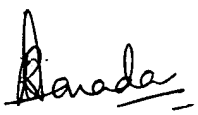
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Lakshmi S Channavajjala
Examiner
Art Unit 1615

August 30, 2003